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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,366	09/19/2003	Fen Huang	34506.143	8954

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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
12/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/666,366	HUANG ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,7-10,14-18,22,24-29,31-35,37-40 and 42-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7-10,14-18,22,24-29,31-35,37-40 and 42-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/21/2007 has been entered.

Applicant's amendment of claims 1, 5, 10, 14, 18, 22, 26, 31, 33, 37, and 42, in the papers of 8/9/2007 and 9/21/2007 , is acknowledged. Applicants' arguments filed on 9/21/2007, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Claims 1, 5, 7-10, 14-18, 22, 24-29, 31-35, 37-40 and 42-45 are still at issue and are present for examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5, 7-10, 14-18, 22, 24-29, 31-35, 37-40 and 42-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art

that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 5, 7-10, 14-18, 22, 24-29, 31-35, 37-40 and 42-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed methods of use of rat or human RNAsin, does not reasonably provide enablement for the claimed methods of use of any RNAase inhibitor protein derived from rats, human placentas, or recombinant human placental sources, in combination with the specified buffer and temperature conditions and having the specified protective results. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The above two rejections were stated in the previous office action as they applied to previous claims 1-45. In response to the rejection applicants have amended claims 1, 5, 10, 14, 18, 22, 26, 31, 33, 37, and 42 and traverse the rejections together as they apply to the newly amended claims.

Applicants submit that because this rejection as well as the rejection below based upon a lack of scope of enablement, are very closely related, they shall be addressed simultaneously.

Applicants submit that these rejections are believed to have been overcome, in major part, by appropriate amendment to the claims. Applicants acknowledge that, in the previous Advisory Action, the Office noted that the claims are enabled and include

descriptive support for "rat or human RNasin.", although applicants acknowledge that applicants representative and the examiner disagrees as to what is meant by "rat or human RNasin".

Applicants submit that the claims have been amended throughout to note that the RNase inhibitor protein is "derived from rats, human placentas, or recombinant human placental sources", which is consistent with applicants representatives interpretation of "rat or human RNasin" but inconsistent with the examiners interpretation of "rat or human RNasin".

Applicants submit that as noted in the application as filed, and in previous arguments submitted by the Applicants, rat-derived RNase inhibitor proteins and human-derived inhibitor proteins are articles of commerce and native human placental RNase inhibitor protein and recombinant human placental RNase inhibitor protein are both available commercially and are well-known, commercial compounds that have been described extensively in both the patent literature and the scientific literature.

Because the claims now positively require that the RNase inhibitor protein is "derived from rats, human placentas, or recombinant human placental sources", Applicants respectfully submit that the rejections under §112, first paragraph (written description and enablement) are untenable and withdrawal of the rejections are respectfully requested.

Applicant's complete argument continues to be acknowledged and has been carefully considered, however, is found nonpersuasive for the reasons previously made of record and repeated herein.

Applicants submission that these rejections are believed to have been overcome, in major part, by appropriate amendment to the claims, that the RNase inhibitor protein is "derived from rats, human placentas, or recombinant human placental sources" is acknowledged, but not in and of itself successful in overcoming the current rejection on the basis that applicants description of a few specific RNAse inhibitor proteins does not describe or enable the scope of the claims drawn to methods of use involving any and all RNAse inhibitor proteins and a specific combination of heat and buffer conditions. While it is noted that a specific rat RNase inhibitor protein and a specific human inhibitor protein are articles of commerce and are well-known, this is not sufficient to describe and enable the claimed methods that read on the use of any RNase inhibitor protein. This interpretation is made based upon applicant's amendment of the claims to recite that the RNase inhibitor proteins of the claimed methods are "derived from rats, human placentas, or recombinant human placental sources".

This interpretation of applicant's newly added recitation "derived from rats, human placentas, or recombinant human placental sources" continues to be based upon applicants previous arguments made in the previous response.

It continues to be of note that applicants have asserted that the shared important structural feature of the referenced RNase inhibitor proteins is that they are merely proteins. This continues to be of concern in applicants intended interpretation of those

RNase inhibitor proteins encompassed by applicant's claims. As has been previously pointed out each of the referenced RNase inhibitors must be a protein, however, this remains an incredibly broad structural genus with respect to the claimed function of RNase inhibition, and even more so when the claimed proteins must maintain this RNase inhibition function in the presence of and thereafter at least 90°C heat. Further applicants are reminded that in addition to the above functions, such a claimed combination must achieve that "RNA present in the mixture or subsequently added to the mixture is protected from enzymatic degradation by Rnases".

As previously stated, the specification also fails to describe additional representative species of RNAase inhibitor proteins for use in the claimed methods by any identifying structural characteristics or properties necessary to ensure the successful use of these inhibitor proteins, i.e. the combination of the RNase inhibitor protein and the specifically recited temperature conditions. Given this lack of additional representative species as encompassed by the claims, and lack of structural to functional characterization, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Further, it continues that one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. This would clearly

constitute undue experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has not been provided in the instant specification. As previously stated the specification does not establish: (A) regions of the protein structure which may be modified without effecting the desired activity(i.e. RNase inhibitor activity in the presence of and thereafter a temperature of 90°C); (B) the general tolerance of any RNAse inhibitor protein to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of any RNAase inhibitor protein with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the necessary activity for the claimed methods and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not, it would require undue experimentation for one skilled in the art to arrive at the majority of those methods of the claimed genus having the desired result.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including those methods of use of any RNase inhibitor protein derived from rat or human, in combination with a temperature of at least

90°C. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10 and 14-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Ambion, Inc. (TechNotes 8(2), SUPERase.In: The Right Choice for Protecting your RNA, web page, www.ambion.com/techlibb/tn/82/823.htm, 10/28/2004, see IDS).

Ambion, Inc. teach a method comprising to a fist solution adding a second solution containing an amount of an RNase inhibitor protein (i.e. SUPERase.In) in a buffer devoid of reducing agents to yield a mixture and heating the mixture to a temperature of 67°C for 15 minutes (See figure 2 and supporting text). The RNase inhibitor SUPERnasin is derived from a mammalian source. And thus the methods taught by Ambion, Inc. anticipate claims 10 and 14-17.

The examiner acknowledges claims 10 and 14-17 were previously left out of this rejection, however, upon further consideration it has been decided that claims 10 and 14-17 should have been included in the rejection, as each of the claimed method steps is taught by the reference, Ambion, Inc.. Any inconvenience to applicants is regretted.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5, 7-10, 14-18, 22, 24-29, 31-35, 37-40 and 42-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mizutani et al. (Microbiol. Immunol., Vol 42 (8), pp 549-553, 1998) and Ambion, Inc. (TechNotes 8(2), SUPERase.In: The Right Choice for Protecting your RNA, web page, www.ambion.com/techlibb/tn/82/823.htm, 10/28/2004, see IDS).

Mizutani et al., disclose single step reverse transcription-polymerase chain reaction for the detection of Hepatitis C virus RNA. Specifically Mizutani et al. teach a method of RT-PCR comprising heating a RNA solution to 95oC for 20 minutes followed by 70 cycles of amplification (See page 550, left column third full paragraph).

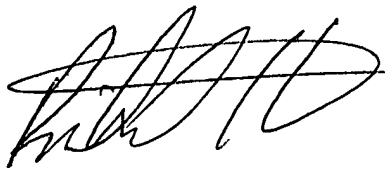
Ambion, Inc. teach a method comprising to a fist solution adding a second solution containing an amount of an RNase inhibitor protein (i.e. SUPERase.In) in a buffer devoid of reducing agents to yield a mixture and heating the mixture to a temperature of 67°C for 15 minutes (See figure 2 and supporting text). The RNase inhibitor SUPERnasin is derived from a mammalian source. Ambion further teach that SUPERnasin does not require DTT to function and inhibits more RNAses, at higher concentrations, under more reaction conditions than other RNase inhibitors. Ambion specifically teach that SUPERnasin is ideal for use in RT-PCR.

One of skill in the art at the time of filing would have been motivated to practice the methods of RT-PCR of Mizutani et al., with the addition of SUPERnasin as taught by Ambion, Inc.. It is noted to applicants that SUPERnasin as taught by Ambion, Inc. is considered to be a "RNase inhibitor protein derived from rats, human placentas or recombinant human placental sources". The motivation for the inclusion of SUPERnasin Ribonuclease inhibitor in the methods of RT-PCR taught by Mizutani et al., is that SUPERnasin inhibits RNases that are known contaminants of RNA preparations. Further SUPERnasin works well in RT-PCR reactions and does not need reducing conditions or reducing agents. The reasonable expectation of success comes from thigh level of skill in the art with respect to PCR amplification technologies and the results of both Mizutani et al., and Ambion, Inc.. Ambion, Inc. specifically teaches that the inclusion of SUPERnasin in RT-PCR reactions is ideal. Thus the methods claimed in claims 1, 5, 7-10, 14-18, 22, 24-29, 31-35, 37-40 and 42-45 are obvious over Mizutani et al. and Ambion, Inc.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
12/5/2007